Informed Consent: The ideal and the reality

Christine Grady

The views expressed here are mine and do not represent the position of the NIH or of the Department of Health and Human Services.

Informed consent

- A legal, regulatory, and ethical requirement of most research with human subjects
- One aspect of conducting ethical clinical research
- A process (not a form or an episode)

The two sense of informed consent

- An autonomous authorization:
  - Informed consent is the intentional authorization of an activity based on substantial understanding and in the absence of control by others
- Social rules of consent
  - An institutionally or legally effective authorization, as determined by prevailing rules
    - Faden and Beauchamp 1986

Ethical basis of informed consent

- Respect for persons
- Respect for individual's capacity and right to define own goals and make choices consistent with these goals
- Well entrenched in American values, jurisprudence, medical practice, and clinical research.

Informed Consent

- Widely subscribed to, but
- Imperfectly realized

Elements of informed consent

- Disclosure of information
- Understanding
- Voluntariness
- Consent authorization

Research on informed consent

- Data on the quality of informed consent
  - Readability of forms
  - Understanding
  - Motivations
- Data comparing consent strategies
  - To improve understanding and satisfaction

Capacity to consent

- Adults generally presumed to have the capacity to consent
- Surrogate decision makers (NIH MAS 87-4)
  - Parents
  - Legal guardians
  - DPAs
- Processes for assessing capacity to consent to research

Elements of informed consent

- **Disclosure of information**
- Understanding
- Voluntariness
- Consent authorization

Disclosure considerations

- What information should be disclosed?
- How should the information be presented?
- Accounting for circumstances and setting?

Disclosure- required elements

(from 45CFR46.116 and 21CFR50.25)

- Statement of research
- Purpose and procedures
- Foreseeable risks and discomforts
- Any benefits to subjects or others
- Appropriate alternatives
- Extent of confidentiality
- Treatment or compensation for injury
- Who to contact for answers to questions
- Participation is voluntary

Informed consent document

- Written in non-technical language that can be easily understood by prospective subjects, consistent with educational level, familiarity with research. (http://ohsr.od.nih.gov/info/sheet6.html)
- Format

- IRB approval of consent document as well as advertisements, fliers, brochures, etc.

Disclosure of information

Setting

Data on disclosure

- Consent documents
  - Readability
  - Content
- Discussion
  - Content
  - Interaction

Consent form readability

- Denver VA (n=88)- mean reading level college; length increased 58% over 7 yrs. LoVerde, 1989
- Phase 1-3 oncology consent forms Johns Hopkins- reading level grade 11 (Flesch-Kincaid) to 14 (Gunning Fog index) Grossman et al, JCO 1994
- Consent templates from websites of 114 US medical schools- average readability score (Flesch-Kincaid) 10.6 grade. Paasche-Orlow et al. NEJM 2003

Reading consent forms

"Hey, no problem!"

Disclosure- content of forms

- 267 Phase I oncology consent forms were found to include:

- The trial was research (99%)
- The purpose as safety testing (92%)
- The right to withdraw (99%)
- Death as a risk (67%), unknown risks (84%)
- Cure as a possible benefit (5%)

Horng et al, NEJM 2002

Disclosure-interaction

- 48 videotaped physician-patient interactions with 12 oncologists were found to include:

- Description of the study purpose (92%)
- Review of the treatments, tests and procedures involved (92%)
- Review of alternatives (82%)

Albrecht et al. 1999

Disclosure practices

- Investigators (n=60) of 12 multi-center RCTs asked about obtaining consent
- 58% reported giving full information, 42% only on the proposed treatment arm
- 12% did not inform patients about the trial prior to randomization
- 38% did not always tell the patient about randomization
- 5% did not seek consent at all

Williams and Zwitter, *Eur J Cancer* 1994

Disclosure practices

- Investigators (n=117) of a multinational HIV trial surveyed about consent practices
  - Provided subject with a copy to read (99%)
  - Subjects had opportunity to read before coming to clinic for signing (97%)
  - Emphasized randomization (<56%)
  - Formal assessment of understanding (8.6%)
    - Sabik et al. IRB 2005

Summary- data on disclosure

- Limited data
- Consent documents seem to include relevant information
- Information is complex
- Disclosure by investigators variable

Elements of informed consent

- Disclosure
- **Understanding**
  - Knowledge of the relevant information
  - Appreciation of how study information applies
- Voluntariness
- Consent

Understanding

- Factors that might affect understanding
- How is understanding assessed?
- How much should subjects understand?
- What happens when subjects don't understand? (or should happen?)

Subject characteristics to consider

- Age
- Severity of illness and need
- Educational level
- Cognitive capacity
- Familiarity with research
- Language and customs
- Capacity for free choice

Data: Understanding research purpose/ nature

- 98% of Swedish women in a gyn trial knew it was research Lynoe et al 1991
- 30% of U.S. Phase I, II, III oncology trial participants knew the treatments were unproven Joffe et al 2001
- 80% of Thai HIV vaccine trial participants knew the vaccine might not work Pitisuttithum et al. 1997
- 100% of participants in a rheumatoid arthritis RCT knew they were in a medical experiment Criscione et al. 2003

Data: Understanding risks/side effects

- 56% of Gambian mothers could name ≥ 1 side effect of HIB vaccine Leach et al, 1999
- 100% of US cancer patients could name ≥ 1 side effect of their Phase I trial Dougherty et al 2000
- 28% of subjects in a Hypertension trial remembered two side effects two hours after consent. Bergler 1980
- 52.4% of subjects in an analgesia study did not remember any of 12 side-effects 60 days after consent. Miller 1994

Data: Understanding Randomization

- 23% of Finnish women in a breast cancer trial remembered that treatment was chosen randomly. Hietanen 2000
- 21% of US IDUs in an HIV vaccine trial knew that not everyone would get the vaccine Harrison et al 1995
- 31% of Thai participants in HIV treatment trial knew that only half would get the experimental treatment Pace et al. 2004
- 42% of US men in beta blocker heart attack trial were aware of the existence of a control group and of the fact that assignment was based on chance Howard 1981

Data: Understanding placebo controls

- 10% of Gambian mothers understood placebo design for vaccine trial Leach et al 1999
- 67% of US participants in a rheumatoid arthritis trial knew that some people would get a placebo, but only 50% knew they were not certain to get active drug, and 53% that treatment would not be decided based on symptoms Criscione et al 2003

Knowledge vs. appreciation

- Therapeutic misconception

- Immediately after consent psychiatric subjects (40%) said assignment would be based on therapeutic needs, and dosage (50%) would be adjusted according to their need. Appelbaum, 1982

Data on what affects understanding

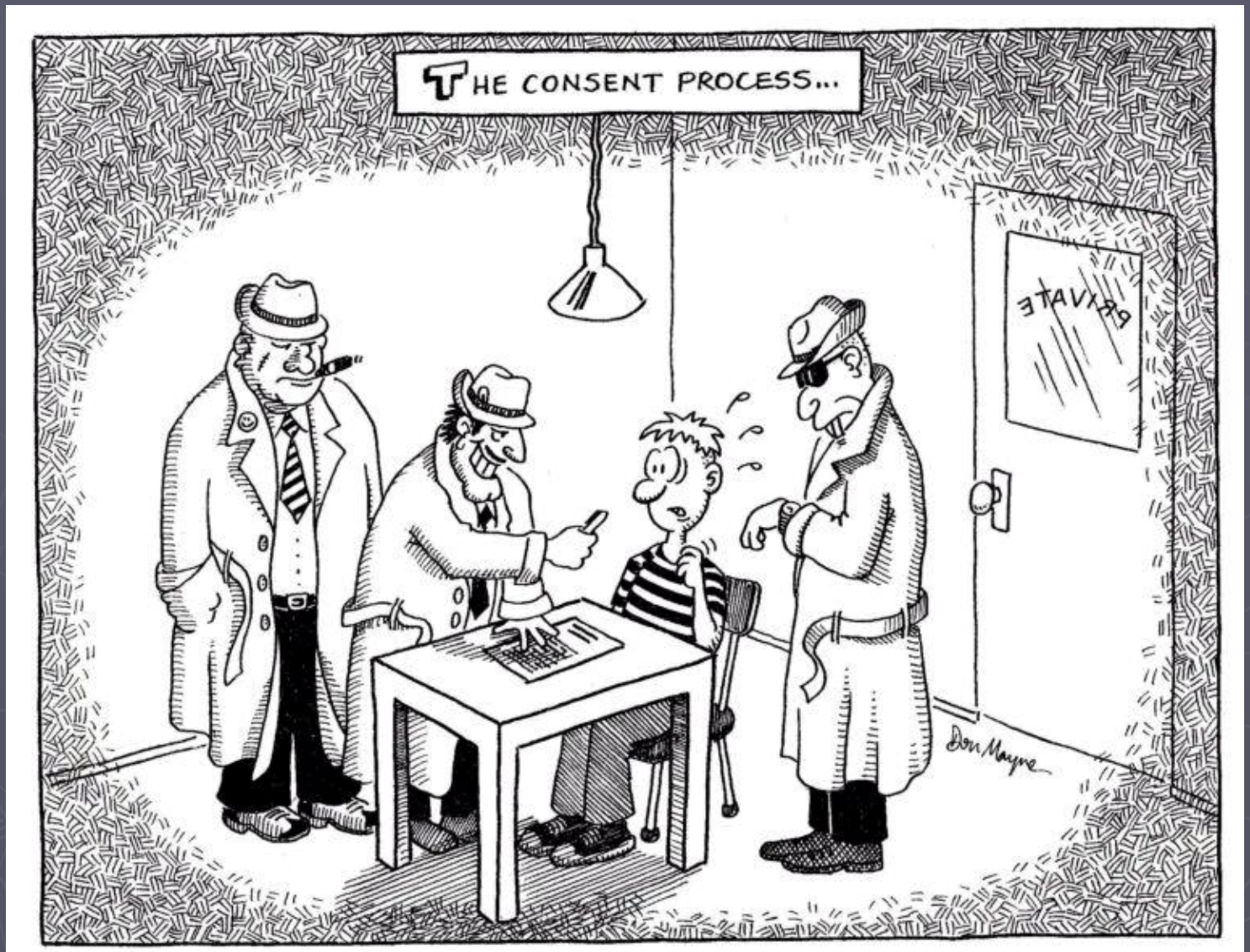
- College education, speaking only English at home Joffe et al 2001
- Education and age Bergler et al 1981
- Education and age Hietanen et al 2000
- Neither education nor age Miller et al. 1994
- Neither education nor previous research experience Pace et al 2003

Summary: data on understanding

- Understanding is variable
- Most subjects know they are in research
- Randomization and placebo are poorly understood
- Understanding =/= appreciation
- Age and education affect understanding, but not always

Voluntariness

- Able to make a (free) choice
- No coercion or undue influence

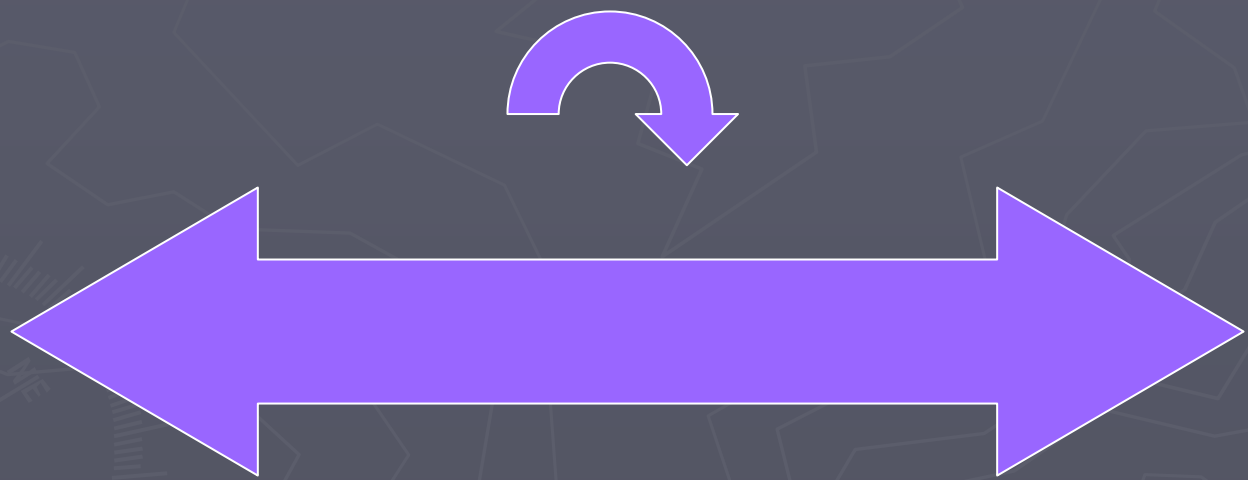


Voluntary participation: possible influences

- Illness
- Restricted choices
- Dependent position
- Trust in health care provider
- Family pressures
- Incentives

Influence

- None ? Controlling



Voluntariness- refusal

- 58% of Guarani Indians refused to participate in a genetics study Benitez 2002
- 43% of adolescents refused participation in an intensive therapy trial for diabetes Terryak et al Diabetes Care 1998
- 9% of women refused participation in breast conserving treatment trial for breast cancer. Bijker et al Brit J Ca 2002

Voluntariness- pressure to join

- 2% of 570 U.S. participants in cardiology and oncology studies felt pressure to join ACHRE 1996
- 25% of Dutch parents of children in an anticonvulsant study “felt obliged” to participate Van Stuijvenberg 1998
- 15% of Ugandan parents felt pressure from others to enroll their child in a malaria treatment trial; 58% felt pressure because of their child’s illness. Pace et al. AJPH 2005

Voluntariness- free to withdraw

- 44% of Swedish women in a gyn trial knew they could quit Lynoe et al 1991
- 96% of US participants in a rheumatoid arthritis study knew they did not have to stay in the trial if they didn't want to Criscione et al 2003
- 93% of South African women in an HIV transmission study knew they were free to quit; but 98% said the clinic would not let them quit Karim 1998

Data: Voluntariness

- 88% of Thai HIV vaccine trial participants knew they could “refuse at any time” Pitisuttithum 1997
- 48% of Bangladeshi pregnant women in an iron supplement trial knew they could quit Lynoe 2001
- 90% of U.S. oncology patients in Phase I, II, or III trials knew they could quit Joffe et al 2001

Consent

- Decision
- Authorization
- Documentation

Consent authorization

- "...informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative" (45CFR46.117, 21CFR50.27)

Consent

- Paraguay: Genetic population study among Guarani Indians with high illiteracy rates
  - Consent form translated to Guarani and read to prospective participants
  - Bilingual Q&A session
  - Participants gave individual oral consent and signed or fingerprinted a written form.
  - All was documented by triple media recording ("audiovisual documentation of consent")

Benitez et al. Lancet 2002; 359: 1406-07

Trials of strategies to improve consent

- Interventions
  - Multimedia (e.g. audiotapes, videotapes, interactive computers)
  - Enhanced consent form (e.g. modified style, format or length)
  - Extended discussion (with team member or neutral educator)
  - Test/feedback (e.g. quizzes and review)

Flory and Emanuel *JAMA* 2004

Trials of strategies to improve consent

- Neither multimedia strategies nor enhanced consent forms consistently improve understanding
  - However, may be as good as usual process
  - May be very appropriate for certain populations
  - May be useful in standardizing disclosure
  - May improve satisfaction

Flory and Emanuel *JAMA* 2004

Trials of strategies to improve consent

- Limited data suggest that more person-to-person contact (through extended discussions, test/feedback strategies, etc.) may help improve understanding

Flory and Emanuel *JAMA* 2004

Trials of strategies to improve consent

"None of the intervention studies clearly identified... methods...to increase knowledge,... satisfaction, or to affect actual decisions"

IRB: Ethics and Human Research Informed consent supplement Sept/Oct. 2003

Informed consent-conclusions

- Informed consent in research is ethically important, but imperfectly realized
- More (and rigorous) data are needed
- Available data suggest:
  - Consent forms are complex, even if complete
  - Participants are generally satisfied
  - Understanding is variable, and lacking in certain areas (e.g. randomization and side effects)
  - Many do not know/feel they can quit
  - Spending more time may enhance understanding